obtained from the parents. The date of the infection could not be determined. Such positive laboratory evidence of past toxoplasmic infection is frequently obtained in persons in an older age group.[2] A negative reaction to a toxoplasma complement-fixation test does not vitiate this observation, since such antibodies seem to disappear shortly after infection or the last contact with the antigen.[13, 3]

SUMMARY

A patient with congenital toxoplasmosis, fatal at five days of age, has been presented. The case is thought to be the earliest on record in the United States. The patient was observed at San Francisco, California, in 1923, and the diagnosis was made recently by finding toxoplasma and specific lesions in the pathologic material saved. Both parents, when examined in 1948, had positive reaction to the toxoplasmin skin test and the toxoplasma neutralizing antibody test.

REFERENCES

1. Cowen, D., Wolf, A., and Paige, B. H.: Toxoplasmic encephalomyelitis. VI. Clinical diagnosis of infantile or congenital toxoplasmosis; survival beyond infancy, Arch. Neurol. & Psychiat., 48:689-739, November 1942.

2. Frenkel, J. K.: Dermal hypersensitivity to toxoplasma antigens (toxoplasmins), Proc. Soc. Exp. Biol. & Med., 68: 634-639, July-August 1948.

3. Frenkel, J. K.: The pathogenesis, diagnosis and treatment of human toxoplasmosis, J.A.M.A., 140:369-377, May 28, 1949.

4. Frenkel, J. K.: Unpublished observations.

5. Jankû, J.: Pathogenesis and pathologic anatomy of coloboma of the macula lutea in an eye of normal dimensions and in a microphthalmic eye with parasites in the retina, Casop. lek. cesk., 62:1021, 1052, 1081, 1111, 1138, 1923.

6. Nicolle, M. M. C., and Manceaux, L.: Sur un protozoaire nouveau du gondi (*Toxoplasma* n.g.), Inst. Pasteur Tunis, Archives, 4:97-103, 1909.

7. Paige, B. H., Cowen, D., and Wolf, A.: Toxoplasmic encephalomyelitis. V. Further observations of infantile toxoplasmosis; intrauterine inception of the disease; visceral manifestations; case 5, Am. J. Dis. Child., 63:474-514, March 1942.

8. Pratt-Thomas, H. R., and Cannon, W. M.: Systemic infantile toxoplasmosis, Am. J. Path., 22:779-795, July 1946.

9. Sabin, A. B.: Toxoplasma neutralizing antibody in human beings and morbid conditions associated with it, Proc. Soc. Exp. Biol. & Med., 51:6-10, 1942.

10. Sabin, A. B.: Toxoplasmosis, a recently recognized disease of human beings, Adv. in Pediatrics, 1:1-60, Interscience Publishers, New York, 1942.

11. Sabin, A. B., and Feldman, H. A.: Dyes as microchemical indicators of a new immunity phenomenon affecting a protozoan parasite (Toxoplasma), Science, 108:660, Dec. 10, 1948.

12. Schwarz, G. A., Rose, E. K., and Fry, W. E.: Toxoplasmic encephalomyelitis. A clinical report of six cases, Pediatrics, 1:478-494, April 1948.

13. Warren, J., and Sabin, A. B.: The complement fixation reaction in toxoplasmic infection, Proc. Soc. Exp. Biol. & Med., 51:11-14, 1942.

14. Weinman, D.: Human toxoplasma, Puerto Rico J. Pub. Health & Trop. Med., 20:125-161, December 1944.

15. Wolf, A., and Cowen, D.: Granulomatous encephalomyelitis due to an encephalitozoon (Encephalitozoic encephalomyelitis). A new protozoan disease of man, Bul. Neur. Inst. N. Y., 6:306-371, July 1937.

16. Zuelzer, W. W.: Infantile toxoplasmosis. With a report of three new cases, including two in which the patients were identical twins, Arch. Path., 38:1-19, July 1944.

# Pancreatic Cysts Simulating Carcinoma of the Head of the Pancreas

## Report of Two Cases

CARLETON MATHEWSON, JR., M.D., and ROY COHN, M.D.,
*San Francisco*

PANCREATICODUODENECTOMY as originally advocated in 1935 by Whipple[1] and his associates for the radical treatment of carcinoma of the papilla of Vater and the head of the pancreas has now become a recognized procedure. Although the early attempts to carry out this radical operation were associated with a high operative mortality, a better understanding of technique and of preoperative and postoperative care have made possible the radical resection of tumors involving the common bile duct, duodenum and head of the pancreas previously considered inoperable.

A number of modifications of the original two-stage operation as performed by Whipple have been made. With the use of vitamin K and blood transfusions to control hemorrhage and anemia, the trend is now toward a one-stage operation. Most surgeons now reimplant the cut end of the pancreas or pancreatic duct into the upper intestine to preserve the external pancreatic secretion, whereas Whipple considered this unnecessary and one of the main hazards of the procedure. Other modifications of the original procedure have to do mainly with the type and position of the anastomosis made to reestablish continuity and still prevent stenosis and troublesome regurgitation of bowel contents into the biliary tree.

With the technical problems solved, the main difficulty confronting the surgeon at present is one of early differential diagnosis. Unfortunately, a number of conditions involving both intra- and extrahepatic biliary passages give rise to similar clinical pictures and are extremely difficult to distinguish one from another. Too often the differential diagnosis is made late and surgical treatment undertaken when surgical extirpation is no longer feasible.

In general, the main consideration in diagnosis involves the differentiation between obstructive and non-obstructive jaundice, which unfortunately is occasionally impossible. In this connection, one must always keep in mind the frequent association of the two, particularly when obstructive jaundice itself has led to secondary degenerative changes in the liver.

Obstructive lesions of the extrahepatic biliary tree, both benign and malignant, although frequently easily distinguished one from the other, may produce clinical pictures so similar that positive differentiation cannot be made without exploratory laparotomy. For this reason it becomes imperative that the surgeon be prepared to recognize and undertake the surgical management of these lesions, regardless of their nature, as they present themselves in the operating room.

Unfortunately, gross and even microscopic examination at the time of operation will not always lead to a positive diagnosis. This is particularly true of obstructing lesions of the lower end of the common bile duct. Often a stone imbedded in the common duct near the ampulla of Vater, with inflammatory reaction about it, will simulate carcinoma. Carcinoma of the ampulla may cause stricture and obstruction without gross evidence of tumor. Inflammatory lesions of the pancreas often cause common duct obstruction and are grossly indistinguishable from carcinoma of the head of the pancreas, even with aid of frozen sections made at the time of operation.

From the Department of Surgery, Stanford University School of Medicine, San Francisco.

Presented before the Section on General Surgery at the 78th Annual Session of the California Medical Association, Los Angeles, May 8-11, 1949.

The purpose of this communication is to report two cases of benign cysts of the head of the pancreas. In one case the cyst was inflammatory in nature, and in the other apparently obstructive in origin. Intermittent obstruction of the common bile duct and jaundice were caused in both cases. The gross pathologic changes in each case at operation were indistinguishable from those of carcinoma of the head of the pancreas. Both of the patients were subjected to radical partial pancreaticoduodenectomy, one in a single-stage operation and the other in a two-stage procedure, under the mistaken diagnosis of carcinoma of the head of the pancreas. Both patients recovered uneventfully from the operation and are living and well.

## CASE REPORTS

CASE 1: The patient, a male 40 years of age, had right subcostal pain radiating to the back, occasional nausea and vomiting and jaundice of eight weeks' duration.

On July 6, 1947, the patient started to have mid-epigastric pain about 4 or 5 p.m. For the next three days he was unable to retain food. There was occasional dull pain in the mid-epigastrium and to the right side, radiating to the back and around the right subcostal margin. At the initial examination the patient was icteric. The liver was slightly enlarged and just barely palpable below the costal margin on the right, and the spleen was not palpable. The icteric index was 55 units. Leukocytes numbered 12,000 with 71 per cent neutrophils and 22 per cent lymphocytes. Result of a test for urobilinogen in the urine was positive in 1:40 dilution. A Wassermann test was negative for syphilis. July 17, the icteric index was 12 units. The cholesterol content in the blood was 233 mg. per 100 cc. and the sugar content 105 mg. per 100 cc. The patient stated that during the first three weeks of hospitalization he had constant nausea and vomiting with pain on the right subcostal margin, radiating to the right side and to the back; and during that time the body weight had decreased 25 pounds. From June 9 to July 26 the temperature ranged between 99° and 100.5°F. daily. On July 29 there was another bout of pain. Leukocytes then numbered 16,800 with 69 per cent neutrophils and 9 per cent stab cells. The icteric index was 16 units, and the result of an indirect van den Bergh test was 6.3 mg. Gastric analysis showed 71 degrees of free acid, the fluid being positive for blood. X-ray studies of the gastrointestinal tract on July 27 revealed no deformities or intrinsic lesions of the stomach. It was felt that there was an extrinsic mass causing a defect of the greater curvature of the stomach. No abnormality was observed in a film of the chest. The gallbladder was visualized. A second gastrointestinal series on August 12 revealed a slight lateral displacement of the duodenum. The radiologist felt that there was an extrinsic mass causing external pressure on the second portion of the duodenum and greater curvature of the stomach. Results of liver function tests were within normal limits.

When the patient first came under the author's observation on September 3, 1947, slight jaundice was noted. The temperature was normal, the pulse rate 80, and the blood pressure 122 mm. of mercury systolic and 80 mm. diastolic. There was some resistance in the right rectus abdominis muscle. Presence of a palpable mass in the right upper quadrant of the abdomen was uncertain.

Results of laboratory tests accorded with those previously carried out.

On September 23 the abdomen was opened through a right subcostal oblique incision. The gallbladder was noted to be rather thickened and with Hartman's pouch settled in a mass of adhesions in the area of the common duct. A wide curve involving the first and second part of the duodenum and over the head of the pancreas was observed. In this curve of the duodenum a hard, irregular mass about the size of a small lemon was felt. It appeared to be fairly well delineated from the body and tail of the pancreas. The tissue circumjacent to this mass, which included the common duct and retroperitoneal tissues, was brawny and edematous as if involved in a prior existent inflammatory process of some type. Frozen section from the mass revealed inflammatory tissue. It was considered that it was best not to take a chance that the mass was totally inflammatory, which meant that a resection should be done. This was accordingly carried out in a single stage partial pancreaticoduodenectomy. Postoperative convalescence was uneventful.

The pathological report was "Pancreatic necrosis with cyst formation and pancreatitis."

* * *

CASE 2: The patient was a male 42 years of age. The chief complaint was progressive jaundice, severe itching of skin and loss of weight over a period of three weeks. The patient had been a heavy drinker for several years but had had no alcohol for the past year.

The last week in December, 1947, diarrhea developed with five or six loose stools daily, normal in color. One week later, jaundice developed with definite fading in color of stools. In January 1948, diarrhea recurred with mild abdominal cramps. The stools were normal in color. In May 1948, progressive painless jaundice with severe itching of the skin developed and there was progressive loss of weight.

Upon physical examination it was noted that the temperature was 97.6°F. and the blood pressure was 138 mm. of mercury systolic and 90 mm. diastolic. There was intense jaundice and the sclerae were jaundiced. The liver edge was palpable two finger-breadths below the right costal margin.

Erythrocytes numbered 4,880,000. The hemoglobin value was 87 per cent. Leukocytes numbered 9,850 with normal differential of cells. There was a trace of albumin in the urine, but no sugar; six to eight leukocytes per high power field were noted, and occasional fine and coarse granular casts. A quantitative urobilinogen test was positive in 1:10 dilution. The icteric index was 50 units. There was 35 per cent retention of Bromsulfalein®. There was positive delayed reaction to van den Bergh's test, and a biphasic direct reaction. A quantitative test for bilirubin showed 1.8 mg. per 100 cc. Result of a cephalin-cholesterol flocculation test was negative. A test of the stool was positive for urobilin, negative for bilirubin.

The abdomen was opened through a right paramedian incision. The liver was found to be normal in size. It was smooth and showed no metastasis. It appeared to be congested with bile. The gallbladder was thin-walled, filled with black bile, and contained no stones. The common duct was thin-walled and distended. No stones were palpated in it. The head of the pancreas was enlarged, being about 2 cm. in diameter, and was very firm. It seemed to be freely movable. The remainder of the pancreas was fairly firm but otherwise normal. The fundus of the gallbladder seemed to lie most easily against the anterior surface of the stomach, so anastomosis was made between the gallbladder and the stomach just proximal to the pylorus. Recovery was uneventful and the jaundice cleared.

At a second operation, with the patient under continuous spinal anesthesia, a transverse upper abdominal incision was made, transecting both recti muscles. The omentum was found adherent to the old upper abdominal scar. After the omentum was freed the previous anastomosis was noted to be intact with very little peritoneal reaction about it. There were a few adhesions between the gallbladder and the transverse colon and between the liver bed and second portion of the duodenum. These were freed and the fingers introduced into the foramen of Winslow. By so doing, a large tumor mass could be felt in the head of the pancreas which seemed to be freely movable. This tumor was thought to be a carcinoma of the pancreas. A partial pancreaticoduodenec-

tomy was performed. The patient made uneventful recovery.

The pathological report was "Cyst, pancreas, simple obstructive; cholecystitis, subacute; lymphadenitis, regional."

### DISCUSSION

In retrospect it might be said that in each of the two cases presented the clinical history might have indicated the true nature of the disease and that the suspicion of carcinoma of the head of the pancreas was unwarranted. Experience has shown, however, that the clinical history is not always to be trusted and that carcinoma of the common duct, carcinoma of the ampulla of Vater and carcinoma of the head of the pancreas may be associated with painless intermittent jaundice, painless constant jaundice and painful intermittent jaundice. Moreover, the pathological findings in each of these cases make it evident that the true nature of the disease could not be determined by gross examination at the time of operation.

### SUMMARY

Two cases of pancreatic cyst causing obstructive jaundice are reported.

Partial pancreaticoduodenectomy was performed in both cases, leading to complete relief of symptoms.

### REFERENCES

1. Whipple, A. O., Parsons, W. B., and Mullins, C. R.: Treatment of carcinoma of the ampulla of Vater, Ann. Surg., 102:763-779, Oct. 1935.

## Anaphylactic Shock Following Intravenous Administration of Thiamine Chloride

### Report of a Case

L. P. ARMANINO, M.D., and W. S. SCOTT, JR., M.D., *Stockton*

RECENTLY, severe reactions to vitamin preparations have been reported in the medical literature.[2, 3, 4, 5, 6, 7] Since these substances are currently popular and are used extensively, and as they may be potentially dangerous when employed indiscriminately, it is fitting to bring forth periodically for consideration by the medical profession certain representative cases of sensitization and to sound a word of caution.

### CASE REPORT

A 39-year-old male had been given two intravenous injections of thiamine chloride for pain in the left shoulder by his wife, a nurse. After the second injection, the patient wheezed and noted some pruritus which disappeared shortly.

At 7 p.m. June 6, 1947, about four months after the second injection, a third injection of 10 mg. of thiamine chloride was administered intravenously. Within two or three minutes, the patient experienced difficulty in breathing and became cyanotic. The skin became cold and moist. The patient then started to wheeze, cough, and expectorate mucus and bloody sputum. He complained of pain in the chest and abdomen. He was hospitalized within an hour, and at this time the skin was ashen. The lungs were full of musical and coarse bubbling rales and coarse rhonchi. The blood pressure was 70 mm. of mercury systolic and 40 mm. diastolic, the pulse rate was 120, respirations 28 per minute, and rectal temperature 97° F. Blood plasma, epinephrine, and oxygen were given immediately. Around 10 p.m. copious, bloody, liquid stools were being passed and the blood pressure was unobtainable. Therapy was continued, and adrenal cortical hormone, vitamin K, and atropine sulfate were added. By 1 a.m. on June 7 the patient's color and pulse had improved, and 5 per cent dextrose in normal saline was substituted for the plasma. At 4 a.m. he was much improved, the blood pressure was 98 mm. of mercury systolic and 70 mm. diastolic, and the pulse rate was 108. The bloody diarrhea and some abdominal cramping persisted, but they seemed relieved by Kaopectate® orally. By noon on June 7, the lungs had cleared, the color of the skin was normal, and the blood pressure was 128 mm. of mercury systolic and 80 mm. diastolic. Later in the afternoon a tarry stool was passed. Up to that time the patient had been given 1,500 cc. of blood plasma, 1,000 cc. of 5 per cent dextrose in normal saline, and 3 cc. of 1:1,000 epinephrine, most of which had been given in the first five hours after entry.

On June 8, 1947, 36 hours after the thiamine chloride injection, the pulse, temperature, respirations, and blood pressure were normal. The patient was taking water by mouth, and was able to breathe outside the oxygen tent without difficulty. He was discharged on June 10 ambulatory and asymptomatic with no gross evidence of blood in the stool.

Subsequent intradermal or passive transfer tests were not carried out. At last report a year later, the patient had remained in good health. There was no history of previous allergic disease in the patient or in his family.

### COMMENT

The profound reaction of this patient to parenteral thiamine chloride was more severe than usual, although deaths from anaphylactic shock have resulted from the use of this drug. The many symptoms are indicative of the widespread involvement of the tissues affected in shock. In addition to circulatory collapse, there was clinical bronchial asthma with pulmonary edema and massive hemorrhage into the gastrointestinal tract. In a case reported by Reingold and Webb[5] microscopic changes noted at autopsy included constriction of the smooth muscle of the pulmonary arteries and bronchioles, which was accompanied by pulmonary engorgement, dilatation of the right side of the heart, and pulmonary emphysema. The presence of pigmented macrophages was thought to indicate that previous hemorrhages had followed an anaphylactizing injection. The veins and sinusoids of the visceral organs were found to be engorged with blood.

In spite of the potential danger of administering vitamin preparations by injection, especially intravenously, apparently this method of administration is widely used. Although such injections may be necessary in selected patients and of psychic advantage in some instances, the oral route remains the cheapest and safest for the great majority of patients.

Every prospective recipient of parenteral vitamin preparations should be quizzed as to sensitivities and reaction to previous similar injections. In addition the use of intracutaneous tests may indicate hypersensitivity to the substances. Even during the using of them, such symptoms as sneezing, wheezing, pruritus, nausea, vomiting, swelling, shortness of breath, nervousness, tachycardia, and collapse should indicate impending danger and perhaps a change in the route of administration of the preparation.

Necessary treatment of reactions depends on the severity of them. In the case here reported, parenteral antihistaminic drugs, which were not available at the time, would have been indicated, in addition to the measures used. In less fulminating cases, epinephrine has proved adequate.[1, 5]

### SUMMARY

A case of anaphylaxis following the intravenous injection of 10 mg. of thiamine chloride is presented. The importance of determining sensitivity prior to parenteral administration of the substance is stressed. Oral administration of vitamins is the safest and preferable in a great majority of subjects. Anaphylactic shock was successfully treated with epinephrine, oxygen, blood plasma, and atropine.

2633 Pacific Avenue.